temperature isomelting domain that is labeled with a detectable label, and where the mutant fraction of each PCR-induced mutation is not greater than about 5×10^{-5};

c) melting and reannealing the product of b) under conditions suitable to form duplexed DNA, thereby producing a mixture of wild type homoduplexes and heteroduplexes which contain point mutations;

d) separating the heteroduplexes from the homoduplexes based upon the differential melting temperatures of said heteroduplexes and said homoduplexes and recovering the heteroduplexes, thereby producing a second pool of DNA that is enriched in target regions containing point mutations;

e) amplifying said second pool in a high fidelity PCR under conditions where only homoduplexed double stranded DNA is produced, thereby producing a mixture of homoduplexed DNA containing wild type target region and homoduplexed DNAs which contain target regions that include point mutations;

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f) resolving the homoduplexed DNAs containing target regions which include point mutations based upon the differential melting temperatures of the DNAs, and recovering the resolved DNAs which contain a target region which includes point mutations; and

g) determining the sequence of the target region of the recovered DNAs to identify point mutations within the target region.---

REMARKS

Claim 26 has been amended and Claim 60 has been added.

Claim 26 has been amended to recite "comparing the age-specific decline determined in e) with the expected age-specific decline of a set of harmful alleles which cause a particular mortal diseases." Support for the amendment is found throughout the specification, for example at page 34, line 2 *et seq.*

Support for Claim 60 is found throughout the specification, for example, at page 17, line 7 *et seq.* Claim 60 is further supported by Claim 1 as filed.

This Preliminary Amendment and Reply to Restriction Requirement adds no new matter to the application.

Reply to Restriction Requirement

Responsive to the Restriction Requirement dated July 19, 2000, Applicant elects the claims of Group II (Claims 23, 25-28, 33, 35, 37, 39, 41, 43, 45, 46, 48, 50, 52 and 59) which the Examiner defines as being drawn to methods for identifying genes with harmful alleles. It is noted that the Group II invention as defined by the Examiner includes claims drawn to a method for identifying genes which carry an allele which increases longevity, a method for identifying genes which affect the incidence of disease, a method for identifying genes which carry deleterious alleles and a method for identifying inherited point mutations which interfere with reproduction, cause or accelerate the appearance of mortal disease or prevent or delay the appearance of a mortal disease. The Examiner is respectfully requested to confirm that such claims are intended to be include in the invention of Group II in the next office communication.

Applicant reserve the right to file a continuing or divisional application or take such other appropriate action as deemed necessary to protect the inventions of Groups I and III. Applicant does not hereby abandon or waive any rights in the inventions of Groups I and III.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

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